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Remarks

The Office Action mailed October 25, 2006 has been received and reviewed. Claims 1-6, 8 and 12-15 are pending. Reconsideration and withdrawal of the rejections are respectfully requested.

Double Patenting Rejections

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798. Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068. Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064. These rejections are respectfully traversed.

The Examiner has improperly relied on the teachings of the instant specification

As previously presented in the Response and Amendment filed August 17, 2006, according to MPEP § 804, "[i]n determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent?" And, while "[a] double patenting rejection of the obviousness-type is 'analogous to . . . the nonobviousness requirement of 35 U.S.C. 103,'" a major distinction is "that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). . . . When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992)."

As previously submitted in the Response and Amendment filed August 17, 2006, and as discussed in more detail below, Applicants continue to submit that the Examiner has improperly relied on the teachings of the instant specification in rejecting the pending claims under the doctrine of obviousness-type double patenting. See, for example, the Examiner's assertions that "the specification indicates UV-irradiation is a major cause of oxidative stress in the cells and may induce apoptosis," (bottom of page 2, Office Action mailed October 25, 2006); that "the specification indicates that colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production" (bridging pages 4-5 and bottom of page 5, Office Action mailed October 25, 2006); and that "the instant specification teaches 4-HNE (4-hydroxynonenal) induces apoptosis . . . and colostrinin inhibits apoptosis in a cell" (page 7, Office Action mailed October 25, 2006). Such reliance on the teachings of the instant specification to substantiate the obviousness of the present claims over issued claims in U.S. Patent Nos. 6,500,798; 6,903,068; and 7,119,064 is improper. Reconsideration and withdrawal of the rejections of the claims under the judicially created doctrine of obviousness-type double patenting is requested.

Applicants submit that, other than passing mention that Applicants have presented this argument, the Examiner has failed to properly respond to this argument (presented herewith and previously presented in the Response and Amendment filed August 17, 2006). Applicants respectfully *insist* that the Examiner fully respond to this argument in the next Office Action.

Obviousness-type double patenting rejection is inconsistent with the Restriction Requirement

The present application was subject to a Restriction Requirement, mailed February 8, 2005. With this Restriction Requirement, the method claims of 1-23 were placed in three different restriction groups, Groups I-III.

Group I included claims 1-11, drawn to a "method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof" and claims 12-15, drawn to a "method for protecting against

DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof."

Group II included claims 16-19, drawn to a "method for reducing the toxic effect of β-amyloid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof."

Group III included claims 20-23, drawn to a "method for reducing the toxic effect of retinoic acid on a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof."

The Examiner asserted that Groups I, II, and III "are distinct from each other *because the methods steps and outcomes are wholly different* among inventions I, II, [and] III . . . and because inventions I-[III] require different searches that are not co-extensive, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper" (page 3, Restriction Requirement mailed February 8, 2005 (emphasis added)).

Applicants elected Group I, with traverse (see Response to Restriction Requirement mailed March 8, 2005). In maintaining the restriction of Groups I-III, the Examiner asserted "coexamination of each of the additional groups . . . would require search of subjects . . . unnecessary for the examination of the elected claims. For example, if Groups II and III were included, it would require additional search of β-amyloid and retinoic acid . . . Therefore, co-examination of each of these inventions would require a serious additional search burden" (page 2, Office Action mailed April 18, 2005).

In view of the Examiner's position that methods "for inhibiting apoptosis in a cell" and "for protecting against DNA damage in a cell" (Group I, original claims 1-15) are patentably distinct from a method "for reducing the toxic effect of β-amyloid on a cell" (Group

II, original claims 16-19) and a method " for reducing the toxic effect of retinoic acid on a cell" (Group III, original claims 20-23), Applicants submit that it is inconsistent for the Examiner to now take the position that the method of Group I is not patentably distinct from a "method for modulating the oxidative stress level in a cell" (claims 1-7 of U.S. Patent No. 6,500,798), a "method for inducing a cytokine in a cell" (claims 1-10 of U.S. Patent No. 6,903,068), and a "method of modulating an intracellular signaling molecule in a cell" (claims 1-7 of U.S. Patent No. 7,119,064). Reconsideration and withdrawal of the rejection of the claims under the judicially created doctrine of obviousness-type double patenting is requested.

Double Patenting Rejection over claims 1-8 of U.S. Patent No. 6,500,798

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798. This rejection is respectfully traversed.

Pending claims 1-6 and 8 are drawn to a "method for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin and combinations thereof . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell." Pending claims 12-15 are drawn to a "method for protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound selected from the group consisting of colostrinin, a constituent peptide of colostrinin, and combinations thereof . . . wherein the compound protects the cell against DNA damage."

Claims 1-7 of U.S. Patent No. 6,500,798 are drawn to a "method for modulating the oxidative stress level in a cell, the method comprising contacting the cell with an oxidative stress regulator under conditions effective to decrease the level of an oxidizing species present in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present; wherein the oxidative stress regulator is colostrinin, a constituent peptide thereof, an active analog of a constituent peptide of colostrinin . . . and combinations

thereof" and claim 8 is drawn to a "method for modulating the oxidative stress level in a cell, the method comprising contacting the cell with an oxidative stress regulator under conditions effective to prevent or reduce an increase in the level of an oxidizing species in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present; wherein the oxidative stress regulator is colostrinin, a constituent peptide thereof, an active analog of a constituent peptide of colostrinin . . . and combinations thereof."

In rejecting pending claims 1-6, 8, and 12-15, the Examiner asserted "the specification indicates UV-irradiation is a major cause of oxidative stress in the cells and may induce apoptosis (Example 8, pages 28-29) . . .[and b]oth sets of claims are directed to a method for inhibiting apoptosis or a method for modulating the oxidative stress level in a cell with an effective amount of colostrinin, a constituent peptide of colostrinin and combinations thereof in response to apoptosis or an oxidative stress such as UV-irradiation " (pages 3-4, Office Action mailed October 25, 2006). Therefore claims 1-6, 8 and 12-15 in the instant application and claims 1-8 of the patent are obvious variations of a method for inhibiting apoptosis or a method for modulating the oxidative stress in a cell." Applicants disagree.

As discussed above, Applicants submit that the Examiner is improperly using the teachings of the specification to substantiate a rejection under the judicially created doctrine of obviousness-type double patenting.

Further, Applicants continue to submit that the Examiner has misinterpreted the teachings of the specification. Example 8 of the specification states that "[b]esides being a major cause of oxidative stress in the cells, UVB-irradiation induces apoptosis by a large number of related pathways such as enhanced Fas transcription and/or mRNA stability, induction of transcriptional factors via c-fos, c-jun, SAP-1 and nuclear factor kB gene expression" (page 29, lines 5-9 of the specification). Applicants submit that the specification discloses that the induction of oxidative stress and the induction of apoptosis are mechanistically separate pathways within the cell, and are not obvious one over the other, as asserted by the Examiner.

In response, the Examiner asserted that "[w]hile induction of oxidative stress by UVB-irradiation and the induction of apoptosis by UVB-irradiation are mechanistically separate pathways within the cells, the UVB-irradiation can cause both oxidative stress and apoptosis" (page 4, Office Action mailed October 25, 2006). Applicants submit that this assertion is based on the Examiner's improper reliance on the teachings of the instant specification.

In maintaining this rejection, the Examiner asserted that the method steps of pending claims 1-6, 8, and 12-15 are the same as the method steps of claims 1-8 of U.S. Patent No. 6,500,798. Applicants disagree. Pending claims 1-6 and 8 are drawn to a "method for inhibiting apoptosis in a cell . . . comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" and pending claims 12-15 are drawn to a "method for protecting against DNA damage in a cell . . . comprising contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage." However, claims 1-7 of U.S. Patent No. 6,500,798 are drawn to a "method for modulating the oxidative stress level in a cell . . . comprising contacting the cell with an oxidative stress regulator under conditions effective to decrease the level of an oxidizing species present in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present" and claim 8 is drawn to a "method for modulating the oxidative stress level in a cell . . . comprising contacting the cell with an oxidative stress regulator under conditions effective to prevent or reduce an increase in the level of an oxidizing species in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present." Applicants submit that the method steps and outcomes of pending claims 1-6, 8, and 12-15 differ from the method steps and outcomes of claims 1-8 of U.S. Patent No. 6,500,798. Thus, the methods cannot be obvious one over the other.

Reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798 is respectfully requested.

Double Patenting Rejection over claims 1-10 of U.S. Patent No. 6,903,068

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068. This rejection is respectfully traversed.

Claims 1-6, 8, and 12-15, drawn to methods for inhibiting apoptosis and protecting against DNA damage, are as summarized above. Claims 1-10 of U.S. Patent No. 6,903,068 are drawn to a "method for inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is selected from the group consisting of a constituent peptide of colostrinin, an active analog thereof, and combinations thereof" (claims 1-5) and a "method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is selected from the group consisting of a constituent peptide of colostrinin, an active analog thereof, and combinations thereof . . . and wherein said active analog modulates an immune response" (claims 6-10).

In rejecting pending claims 1-6, 8, and 12-15 as "obvious variations" of claims 1-10 of U.S. Patent No. 6,903,068, the Examiner continues to assert that "the specification indicates that colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production (page 8, lines 11-15; page 22, lines 32-33; page 29, lines 24-30)" (see pages 4-5, Office Action mailed October 25, 2006). Applicants submit that the Examiner is inappropriately relying on the teachings of the currently pending specification to substantiate a rejection under the judicially created doctrine of obviousness-type double patenting. Further, Applicants submit

that the present methods of claims 1-6, 8, and 12-15 are patentably distinct from the methods of claims 1-10 of U.S. Patent No. 6,903,068.

In maintaining this rejection, the Examiner asserted that the method steps of pending claims 1-6, 8, and 12-15 are the same as the method steps of claims 1-10 of U.S. Patent No. 6,903,068. Applicants disagree. Pending claims 1-6 and 8 are drawn to a "method for inhibiting apoptosis in a cell . . . comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" and pending claims 12-15 are drawn to a "method for protecting against DNA damage in a cell . . . comprising contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage." However, claims 1-10 of U.S. Patent No. 6,903,068 are drawn to a "method for inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is selected from the group consisting of a constituent peptide of colostrinin, an active analog thereof, and combinations thereof" (claims 1-5) and a "method for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine, wherein the immunological regulator is selected from the group consisting of a constituent peptide of colostrinin, an active analog thereof, and combinations thereof . . . and wherein said active analog modulates an immune response" (claims 6-10). Applicants submit that the method steps and outcomes of pending claims 1-6, 8, and 12-15 differ from the method steps and outcomes of claims 1-10 of U.S. Patent No. 6,903,068. Thus, the methods cannot be obvious one over the other.

Reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068 is respectfully requested.

Double Patenting Rejection over claims 1-7 of U.S. Patent No. 7,119,064

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064. This rejection is respectfully traversed.

Claims 1-6, 8, and 12-15, drawn to methods for inhibiting apoptosis and protecting against DNA damage, are as previously summarized. Claims 1-7 of U.S. Patent No. 7,119,064 are drawn to a "method of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin, and combinations thereof, under conditions effective to accomplish at least one of the following: reduce 4-hydroxynonenal (4HNE)-protein adduct formation; inhibit 4HNE-mediated glutathione depletion; inhibit 4HNE-induced activation of p53 protein; or inhibit 4HNE-induced activation of c-Jun NH2-terminal kinases" (claims 1-6) and a "method of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin, and combinations thereof . . . wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated" (claim 7).

In rejecting pending claims 1-6, 8, and 12-15, the Examiner asserted that "the specification indicates 4-HNE (4-hydroxynonenal) induces apoptosis (Example 7, page 28)" (page 7, Office Action mailed October 25, 2006) and thus, the presently claimed method for inhibiting apoptosis and for protecting against DNA damage are "obvious variations" of the methods of claims 1-7 of U.S. Patent No. 7,119,064. Applicants disagree. Applicants respectfully submit that the Examiner is inappropriately relying on the teachings of the currently pending specification to substantiate a rejection under the judicially created doctrine of obviousness-type double patenting. Further, Applicants submit that the present methods of

claims 1-6, 8, and 12-15 are patentably distinct from the methods of claims 1-7 of U.S. Patent No. 7,119,064.

In maintaining this rejection, the Examiner asserted that the method steps of pending claims 1-6, 8, and 12-15 are the same as the method steps of claims 1-7 of U.S. Patent No. 7,119,064. Applicants disagree. Pending claims 1-6 and 8 are drawn to a "method for inhibiting apoptosis in a cell . . . comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" and pending claims 12-15 are drawn to a "method for protecting against DNA damage in a cell . . . comprising contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage." However, 1-7 of U.S. Patent No. 7,119,064 are drawn to a "method of modulating an intracellular signaling molecule in a cell . . .comprising contacting the cell with an effective amount of a modulator . . . under conditions effective to accomplish at least one of the following: reduce 4-hydroxynonenal (4HNE)-protein adduct formation; inhibit 4HNE-mediated glutathione depletion; inhibit 4HNE-induced activation of p53 protein; or inhibit 4HNE-induced activation of c-Jun NH2-terminal kinases" (claims 1-6) and a "method of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with lipid peroxidation in a cell . . . comprising contacting the cell with an effective amount of a modulator selected . . . wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated" (claim 7). Applicants submit that the method steps and outcomes of pending claims 1-6, 8, and 12-15 differ from the method steps and outcomes of claims 1-7 of U.S. Patent No. 7,119,064. Thus, the methods cannot be obvious one over the other.

Reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064 is respectfully requested.

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Summary

It is respectfully submitted that the pending claims 1-6, 8 and 12-15 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 22nd day of December, 2006, at 8:45 am (Central Time).

By: Danielle N. Morris
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